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Docket No.: 066783-0144

PATENT

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

Applicant : KOEFFLER, H. Phillip, et al.
Appl. No. : 10/756,890
Filed : January 13, 2004
Title : PARICALCITOL AS A
CHEMOTHERAPEUTIC AGENT
Grp./A.U. : 1632
Examiner: : NOT YET ASSIGNED

Customer No.: 41552
Confirmation No.: 3623

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Kate Lane
Kate Lane

Commissioner for Patents
P.O. Box 1450
Alexandria, VA 22313-1450

Dear Sir:

Transmitted herewith is an Information Disclosure Statement in the above-identified application.

Also attached: 1 Information Disclosure Listing of Reference
77 References

The Commissioner is hereby authorized to charge payment of any fees associated with this communication or credit any overpayment, to Deposit Account No. 502624, including any filing fees under 37 CFR 1.16 for presentation of extra claims and any patent application processing fees under 37 CFR 1.17.

Respectfully submitted,

MCDERMOTT WILL & EMERY LLP

Deborah L. Cadena

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INFORMATION DISCLOSURE STATEMENT

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Dear Sir:

In accordance with the provisions of 37 C.F.R. 1.56, 1.97 and 1.98, the attention of the Patent and Trademark Office is hereby directed to the documents listed on the attached form PTO-1449. It is respectfully requested that the documents be expressly considered during the prosecution of this application, and that the documents be made of record therein and appear among the "References Cited" on any patent to issue therefrom.

This Information Disclosure Statement is being filed within three months of the U.S. filing date OR before the mailing date of a first Office Action on the merits. No certification or fee is required.

Serial No.: 10/756,890

One English language reference was cited in a corresponding foreign application search report and its relevance discussed therein. A copy of the foreign search report is attached for the Examiner's information.

Please charge any shortage in fees due in connection with the filing of this paper, including extension of time fees, to Deposit Account 502624 and please credit any excess fees to such deposit account.

Respectfully submitted,

McDERMOTT WILL & EMERY LLP

A handwritten signature in black ink, appearing to read "Deborah L. Cadena". The signature is fluid and cursive, with the first name being the most prominent.

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U.S. PATENT DOCUMENTS

EXAMINER'S INITIALS	CITE NO.	Document Number Number-Kind Code2 (if known)	Publication Date MM-DD-YYYY	Name of Patentee or Applicant of Cited Document	Pages, Columns, Lines, Where Relevant Passages or Relevant Figures Appear
	1	US 6,624,138	09-23-2003	SUNG et al.	
	2	US 5,976,784	11-02-1999	DeLUCA et al.	
	3	US 5,952,317	09-14-1999	DeLUCA et al.	
	4	US 5,942,502	08-24-1999	DeLUCA et al.	
	5	US 5,716,946	02-10-1998	DeLUCA et al.	
	6	US 5,597,815	01-28-1997	DeLUCA et al.	
	7	US 5,571,802	11-06-1996	DeLUCA et al.	

FOREIGN PATENT DOCUMENTS

EXAMINER'S INITIALS	CITE NO.	Foreign Patent Document Country Codes-Number 4-Kind Codes (if known)	Publication Date MM-DD-YYYY	Name of Patentee or Applicant of Cited Document	Pages, Columns, Lines Where Relevant Figures Appear	Translation Yes No

OTHER ART (Including Author, Title, Date, Pertinent Pages, Etc.)

EXAMINER'S INITIALS	CITE NO.	Include name of the author (in CAPITAL LETTERS), title of the article (when appropriate), title of the item (book, magazine, journal, serial, symposium, catalog, etc.), date, page(s), volume-issue number(s), publisher, city and/or country where published.
	8	ABE et al., "A novel vitamin D3 analog, 22-oxa-1,25-dihydroxyvitamin D3, inhibits the growth of human breast cancer in vitro and in vivo without causing hypercalcemia," <u>Endocrinology</u> 129:832-837 (1991)
	9	AGGERHOLM et al., "Mutational analysis of the tumour suppressor gene MMAC1/PTEN in malignant myeloid disorders," <u>Eur. Journal of Haematology</u> 65:109-113 (2000)
	10	ANZANO et al., "1 alpha,25-Dihydroxy-16-ene-23-yne-26,27-hexafluorocholecalciferol (Ro24-5531), a new deltanoid (vitamin D analogue) for prevention of breast cancer in the rat," <u>Cancer Res.</u> 54(7):1653-1656 (1994)
	11	BC CANCER AGENCY: CARE AND RESEARCH, "Unconventional Therapies- Vitamin D/Cholecalciferol/Calcitriol," http://www.bccancer.bc.ca/PPI/UnconventionalTherapies/VitaminDCholecalciferolCalcitriol.htm (2000)

EXAMINER

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INFORMATION DISCLOSURE CITATION IN AN APPLICATION		ATTY. DOCKET NO. 066783-0144	SERIAL NO. 10/756,890
		APPLICANT KOEFFLER, H. Phillip, et al.	
		FILING DATE January 13, 2004	GROUP 1632
	12	BENNETT et al., "Proposals for the classification of the myelodysplastic syndromes," <u>Br. J. Haematol.</u> 51(2):189-199 (1982)	
	13	CAMPBELL et al., "Vitamin D3 analogs and their 24-oxo metabolites equally inhibit clonal proliferation of a variety of cancer cells but have differing molecular effects," <u>J. Cell. Biochem.</u> 66:413-425 (1997)	
	14	CANTLEY and NEEL, "New insights into tumor suppression: PTEN suppresses tumor formation by restraining the phosphoinositide 3-kinase/AKT pathway," <u>Proc. Natl. Acad. Sci. USA</u> 96:4240-4245 (1999)	
	15	CASTAIGNE et al., "All-Trans Retinoic Acid as a Differentiation Therapy for Acute Promyelocytic Leukemia. I. Clinical Results," <u>Blood</u> 76(9):1704-1709 (1990)	
	16	CHEN et al., "Evaluation of vitamin D analogs as therapeutic agents for prostate cancer," <u>Recent Results Cancer Res.</u> 164:273-288 (2003)	
	17	CHEN et al., "The in Vitro Evaluation of 25-Hydroxyvitamin D ₃ and 19-nor-1 α ,25-Dihydroxyvitamin D ₂ as Therapeutic Agents for Prostate Cancer," <u>Clinical Cancer Research</u> 6(3):901-908 (2000)	
	18	CHRISTOFORI and SEMB, "The role of the cell-adhesion molecule E-cadherin as a tumour-suppressor gene," <u>Trends Biochem. Sci.</u> 24:73-76 (1999)	
	19	DAHIA et al., "PTEN is inversely correlated with the cell survival factor Akt/PKB and is inactivated via multiple mechanisms in haematological malignancies," <u>Hum. Mol. Genet.</u> 8:185-193 (1999)	
	20	DANIELPOUR et al., "Development and characterization of nontumorigenic and tumorigenic epithelial cell lines from rat dorsal-lateral prostate," <u>Cancer Res.</u> 54(13):3413-3421 (1994)	
	21	De VOS et al., "Effects of potent vitamin D3 analogs on clonal proliferation of human prostate cancer cell lines," <u>Prostate</u> 31(2):77-83 (1997)	
	22	Di CRISTOFANO and PANDOLFI, "The multiple roles of PTEN in tumor suppression," <u>Cell</u> 100(4):387-390 (2000)	
	23	Di CRISTOFANO et al., "Pten is essential for embryonic development and tumour suppression," <u>Nat. Genet.</u> 19(4):348-355 (1998)	
	24	DOGLIONI et al., "p21/WAF1/CIP1 expression in normal mucosa and in adenomas and adenocarcinomas of the colon: its relationship with differentiation," <u>J. Pathol.</u> 179(3):248-253 (1996)	
	25	DUNLAP et al., "1 α ,25-dihydroxyvitamin D(3) (calcitriol) and its analogue, 19-nor-1 α ,25(OH)(2)D(2), potentiate the effects of ionising radiation on human prostate cancer cells," <u>British Journal of Cancer</u> 89(4):746-753 (2003)	
	26	FOSSLIEN, "Biochemistry of cyclooxygenase (COX)-2 inhibitors and molecular pathology of COX-2 in neoplasia," <u>Crit. Rev. Clin. Lab. Sci.</u> 37(5):431-502 (2000)	
	27	GUMBINER, "Cell adhesion: the molecular basis of tissue architecture and morphogenesis," <u>Cell</u> 84(3):345-357 (1996)	
EXAMINER		DATE CONSIDERED	

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	28	GUANTI et al., "Involvement of PTEN mutations in the genetic pathways of colorectal cancerogenesis," <u>Human Mol. Genetics</u> 9(2):283-287 (2000)	
	29	GUPTA and DUBOIS, "Colorectal cancer prevention and treatment by inhibition of cyclooxygenase-2," <u>Nat. Rev. Cancer</u> 1(1):11-21 (2001)	
	30	HARRISON et al., "1,25-dihydroxyvitamin D(3)-induced retardation of the G(2)/M traverse is associated with decreased levels of p34(cdc2) in HL60 cells," <u>J. Cell. Biochem.</u> 75(2):226-234 (1999)	
	31	HE et al., "Identification of c-MYC as a target of the APC pathway," <u>Science</u> 281(5382):1509-1512 (1998)	
	32	HISATAKE et al., "5,6-trans-16-ene-vitamin D3: a new class of potent inhibitors of proliferation of prostate, breast, and myeloid leukemic cells," <u>Cancer Res.</u> 59(16):4023-4029 (1999)	
	33	HISATAKE et al., "Novel vitamin D(3) analog, 21-(3-methyl-3-hydroxy-butyl)-19-nor D(3), that modulates cell growth, differentiation, apoptosis, cell cycle, and induction of PTEN in leukemic cells," <u>Blood</u> 97(8):2427-2433 (2001)	
	34	HUANG et al., "Use of all-trans retinoic acid in the treatment of acute promyelocytic leukemia," <u>Blood</u> 72(2):567-572 (1988)	
	35	HUANG et al., "The antiproliferative effect of paricalcitol and its interaction with cisplatin in head and neck squamous cell carcinomas," <u>Proc. Am. Soc. Clin. Oncol.</u> 22:509 (2003)	
	36	HUERTA et al., "1alpha,25-(OH)(2)-D(3) and its synthetic analogue decrease tumor load in the Apc(min) Mouse," <u>Cancer Res.</u> 62:741-746 (2002)	
	37	JIANG et al., "Induction of differentiation in human promyelocytic HL-60 leukemia cells activates p21, WAF1/CIP1, expression in the absence of p53," <u>Oncogene</u> 9:3397-3406 (1994)	
	38	JONES et al., "Current understanding of the molecular actions of vitamin D," <u>Physiol. Rev.</u> 78(4):1193-1231 (1998)	
	39	JUNG et al., "1,25(OH)2-16ene-vitamin D3 is a potent antileukemic agent with low potential to cause hypercalcemia," <u>Leuk. Res.</u> 18(6):453-463 (1994)	
	40	KOEFFLER et al., "Lymphocyte cell lines from vitamin D-dependent rickets type II show functional defects in the 1 alpha,25-dihydroxyvitamin D3 receptor," <u>Mol. Cell. Endocrinology</u> 70(1):1-11 (1990)	
	41	KOIKE et al., "19-nor-hexafluoride analogue of vitamin D3: a novel class of potent inhibitors of proliferation of human breast cell lines," <u>Cancer Res.</u> 57(20):4545-4550 (1997)	
	42	KRISHNAN, "The role of vitamin D in prostate cancer," <u>Recent Results Can. Res.</u> 164:205-221 (2003)	
	43	KUBOTA et al., "19-nor-26,27-bishomo-vitamin D3 analogs: a unique class of potent inhibitors of proliferation of prostate, breast, and hematopoietic cancer cells," <u>Cancer Res.</u> 58(15):3370-3375 (1998)	

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	44	KUMAGAI, et al., "Vitamin D2 analog 19-nor-1,25-dihydroxyvitamin D2: antitumor activity against leukemia, myeloma, and colon cancer cells," <u>J. of the Natl. Cancer Inst.</u> 95(12):896-905 (2003)	
	45	LEVY et al., "The novel analog 1,24(S)-dihydroxyvitamin D2 is as equipotent as 1,25-dihydroxyvitamin D3 in growth regulation of cancer cell lines," <u>Anticancer Res.</u> 18(3A):1769-1775 (1998)	
	46	LI et al., "PTEN, a putative protein tyrosine phosphatase gene mutated in human brain, breast, and prostate cancer," <u>Science</u> 275(5308):1943-1947 (1997)	
	47	LIU et al., "Mutation analysis of PTEN/MMAC1 in acute myeloid leukemia," <u>Am. J. Hematol.</u> 63(4):170-175 (2000)	
	48	LLACH et al., "Suppression of parathyroid hormone secretion in hemodialysis patients by a novel vitamin D analogue: 19-nor-1,25-dihydroxyvitamin D2," <u>Am. J. Kidney Dis.</u> 32(2 Suppl. 2): S48-54 (1998)	
	49	MARTIN et al., "19-Nor-1-alpha-25-dihydroxyvitamin D2 (Paricalcitol) safely and effectively reduces the levels of intact parathyroid hormone in patients on hemodialysis," <u>J. Am. Soc. Nephrol.</u> 9(8):1427-1432 (1998)	
	50	MILLER et al., "Vitamin D receptor expression, 24-hydroxylase activity, and inhibition of growth by 1alpha,25-dihydroxyvitamin D3 in seven human prostatic carcinoma cell lines," <u>Clin. Cancer Res.</u> 1(9):997-1003 (1995)	
	51	MUNKER et al., "A new series of vitamin D analogs is highly active for clonal inhibition, differentiation, and induction of WAF1 in myeloid leukemia," <u>Blood</u> 88(6):2201-2209 (1996)	
	52	NEPHROLOGY PHARMACY ASSOCIATES, Inc.: Drug Information for Dialysis Units, "New Vitamin D Therapies for Secondary Hyperparathyroidism: Hormone Versus Prohormone," http://www.nephrologypharmacy.com/downloads/Medfacts1-3.pdf (1999)	
	53	NORMAN et al., "1,25(OH)2-vitamin D3, a steroid hormone that produces biologic effects via both genomic and nongenomic pathways," <u>J. Steroid Biochem. Mol. Biol.</u> 41(3-8):231-240 (1992)	
	54	OBATA et al., "Frequent PTEN/MMAC mutations in endometrioid but not serous or mucinous epithelial ovarian tumors," <u>Cancer Res.</u> 58(10):2095-2097 (1998)	
	55	OHYAMA et al., "Identification of a vitamin D-responsive element in the 5'-flanking region of the rat 25-hydroxyvitamin D3 24-hydroxylase gene," <u>J. Biol. Chem.</u> 269(14):10545-10550 (1994)	
	56	O'KELLY et al., "Normal myelopoiesis but abnormal T lymphocyte responses in vitamin D receptor knockout mice," <u>J. Clin. Invest.</u> 109(8):1091-1099 (2002)	
	57	OSHIMA et al., "Suppression of intestinal polyposis in Apc delta716 knockout mice by inhibition of cyclooxygenase 2 (COX-2)," <u>Cell</u> 87(5):803-809 (1996)	
	58	PAKKALA et al., "Vitamin D3 analogs: effect on leukemic clonal growth and differentiation, and on serum calcium levels," <u>Leuk. Res.</u> 19(1):65-72 (1995)	

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	59	PALMER et al., "Vitamin D(3) promotes the differentiation of colon carcinoma cells by the induction of E-cadherin and the inhibition of beta-catenin signaling," <u>J. Cell. Biol.</u> 154(2):369-387 (2001)	
	60	PARK et al., "Induction of apoptosis by vitamin D3 analogue EB1089 in NCI-H929 myeloma cells via activation of caspase 3 and p38 MAP kinase," <u>Br. J. Haematology</u> 109(3):576-583 (2000)	
	64	PERL et al., "A causal role for E-cadherin in the transition from adenoma to carcinoma," <u>Nature</u> 392(6627):190-193 (1998)	
	62	POLAKIS, "Wnt signaling and cancer," <u>Genes Dev.</u> 14(15):1837-1851 (2000)	
	63	REICHRATH, "Will Analogs of 1,25-dihydroxyvitamin D(3) (calcitriol) Open a New Era in Cancer Therapy," <u>Onkologie</u> 24:128-133 (2001)	
	64	RISTIMAKI et al., "Prognostic significance of elevated cyclooxygenase-2 expression in breast cancer," <u>Cancer Res.</u> 62(3):632-635 (2002)	
	65	SAKAI et al., "PTEN gene alterations in lymphoid neoplasms," <u>Blood</u> 92(9):3410-3415 (1998)	
	66	SEIBERT et al., "Distribution of COX-1 and COX-2 in normal and inflamed tissues," <u>Adv. Exp. Med. Biol.</u> 400A:167-170 (1997)	
	67	SIEBERT et al., "Actions of vitamin D3, analogs on human prostate cancer cell lines: comparison with 1,25-dihydroxyvitamin D3," <u>Adv. Prostaglandin Thromboxane Leukot. Res.</u> 23(6):125-127 (1995)	
	68	SKOWRONSKI et al., "Actions of vitamin D3, analogs on human prostate cancer cell lines: comparison with 1,25-dihydroxyvitamin D3," <u>Endocrinology</u> 136(1):20-26 (1995)	
	69	SLATOPOLSKY et al., "Should Vitamin D Analogs be the Therapy of Preference for ESRD Patients with Secondary Hyperparathyroidism," <u>Dialysis and Transplantation</u> 30(4):190-195 (2001)	
	70	SMITH et al., "Pharmacological analysis of cyclooxygenase-1 in inflammation," <u>Proc. Natl. Acad. Sci. USA</u> 95(22):13313-13318 (1998)	
	71	STEINBACH et al., "The effect of celecoxib, a cyclooxygenase-2 inhibitor, in familial adenomatous polyposis," <u>New England J. Medicine</u> 342(26):1946-1952 (2000)	
	72	STRAX, "Vitamin D Hormone Mimic May Boost Effectiveness of Radiation Therapy for Prostate Cancer," PSA Rising: Prostate Cancer Survivor, News, Info & Support, http://psa-rising.com/med/zemplarvitdwakef082003.shtm (2003)	
	73	SUZUKI et al., "High cancer susceptibility and embryonic lethality associated with mutation of the PTEN tumor suppressor gene in mice," <u>Curr. Biol.</u> 8(21):1169-1178 (1998)	
	74	TAKEICHI, "Morphogenetic roles of classic cadherins," <u>Curr. Opin. Cell Biol.</u> 7(5):619-627 (1995)	
	75	TASHIRO et al., "Mutations in PTEN are frequent in endometrial carcinoma but rare in other common gynecological malignancies," <u>Cancer Res.</u> 57(18):3935-3940 (1997)	
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